

gation of auditory verbal imagery and language perception in relation to hallucinations.

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References

1. Ait Bentaleb L, Beauregard M, Liddle P, Stip E. Cerebral activity associated with auditory verbal hallucinations: a functional magnetic resonance imaging case study. *J Psychiatry Neurosci* 2002;27:110-5.
2. Sommer IEC, Aleman A, Ramsey NF, Bouma A, Kahn RS, Handedness, language lateralisation and anatomical asymmetry in schizophrenia; a meta-analysis. *Br J Psychiatry* 2001;178:344-51.
3. Sommer IEC, Ramsey NF, Kahn RS. Lateralization in schizophrenia: an fMRI study. *Schizophr Res* 2001;52:57-67.
4. McGuire PK, Silbersweig DA, Wright I, Murray RM, Frackowiak RS, Frith CD. The neural correlates of inner speech and auditory verbal imagery in schizophrenia: relationship to auditory verbal hallucinations. *Br J Psychiatry* 1996;169(2):148-59.
5. Woodruff P, Brammer M, Mellers J, Wright I, Bullmore E, Williams S. Auditory hallucinations and perception of external speech [letter]. *Lancet* 1995;346(8981):1035.
6. Lennox BR, Park SBG, Medley I, Morris PG, Jones PB. The functional anatomy of auditory hallucinations in schizophrenia. *Psychiatry Res* 2000;100:13-20.
7. Silbersweig DA, Stern E, Frith C, Cahill C, Holmes A, Grootenk S, et al. A functional neuroanatomy of hallucinations in schizophrenia. *Nature* 1995;378:176-9.
8. Dierks T, Linden DJE, Jandl M, Formisano E, Goebel R, Lanfermann H, et al. Activation of Heschl's gyrus during auditory hallucinations. *Neuron* 1999;22:615-21.
9. Shergill SS, Brammer MJ, Williams SCR, Murray RM, McGuire PK. Mapping auditory hallucinations in schizophrenia using functional magnetic resonance imaging. *Arch Gen Psychiatry* 2000;57:1033-8.

The authors respond:

We would like to thank Sommer and colleagues for their comments regarding our article and for their meta-analysis of research into the lateralization of verbal hallucinations.¹ However, we believe that it is difficult on the basis of a meta-analysis alone to settle, once and for all, the issue of the lateralization of hallucinations.

First, 2 types of experimental paradigms have proved instructive regarding cerebral functions affected by schizophrenic hallucinations: (1) those where cerebral activity in the presence of a specific hallucination is compared with the activity that occurs in its absence; and (2) those where the cerebral activity that occurs during the performance of a specific task involving lexical or auditory data processing is compared with the activity that occurs when the participant is in a defined controlled state that clearly differs from the state under study. In each of these paradigms, if we wish to arrive at a sound interpretation of the data, measures must be taken to control the numerous sources of fluctuations in cerebral activity that could easily skew matters. Consequently, the studies to date have necessarily been heterogeneous, thereby complicating any meta-analysis.

Second, reviewing the conclusions drawn in functional imaging studies, we notice that anomalies have been observed in several regions of the brain, but there is no evidence of the worsening of a function located consistently in one or other of these. The problem appears to stem rather from an abnormal coordination of brain activa-

tion in various sites. In other words, we should be focusing more on connectivity than on lateralization.

Third, it seems conceivable that certain functional connectivity anomalies in the cortical regions could serve as relatively stable features capable of characterizing the disease, whereas others are transitory phenomena characteristic of a particular state. In this regard, certain observations suggest that during the acute stage of the illness, a generalized deficit occurs in the functioning of the 2 hemispheres, but particularly in the right. After remission, however, disturbances persist only in the left.² Any meta-analysis must take this into account.

Finally, it is useful to refer to a theory of language such as access to the mental lexicon (contribution of the left hemisphere), which calls for experimental paradigms such as those used for lexical decisions. The 2 hypotheses currently most studied to explain the genesis of auditory hallucinations are (1) an internal discourse not recognized as his own by the hallucinating subject and (2) aberrant activity accessing the primary auditory area. In most cases, the verbal content of auditory hallucinations remains the same from 1 psychotic episode to the next, even when the 2 episodes are separated by a long period of remission. This has led us to hypothesize that the verbal content of auditory hallucinations persists at a subclinical level even during periods of full remission and is quickly reactivated when the subject is exposed to stressful events. We also suggest that these 2 hypotheses apply above all to this specific verbal content.

To test these assumptions, we

used a lexical decision task with 12 right-handed adults (6 patients and 6 controls). The patients (3 men and 3 women) suffered from paranoid schizophrenia as per the DSM-IV criteria but had been well stabilized for at least 6 months. All had a history of auditory hallucinations, with at least 2 acute psychotic episodes of schizophrenia during which they presented the same verbal hallucinatory content. Moreover, at the time of the study, patients had not experienced a hallucination for at least 6 months.

The controls (3 men and 3 women) were matched to the patients. Two lists of words (H and A) and 2 lists of non-words (NH and NA) were used with each patient-control pair. The H list consisted of words from the verbal content hallucinated by a given patient during at least 2 psychotic episodes separated by at least 6 months' remission. The A list was made up of words matched with those of the H list on the basis of length, semantic content, affective valence, abstract-concrete dimension and frequency of use, as per the word frequency dictionary by Jean Beaudot.³ The stimuli (i.e., words from the H, A, NH and NA lists) were constructed on the basis of the hallucinatory content of a given patient (H list). They were used with the patient in question and his/her control alone. In other words, we constructed 6 groups of stimuli, each group being specific to a patient-control pair.

The stimuli were represented by black characters (Geneva 44 font) on a white background. They were presented on a computer screen and remained there until the subject responded. Once a response was given, the second stimulus appeared on the screen after a delay of 499 ms. The stimuli were presented in random order except that no more than 3 stimuli from the same list could be presented in a row, as has been the practice in most lexical decision studies. Before beginning, the subjects underwent brief training with non-experimental lists to familiarize themselves with the task. They were told to press the right arrow of the computer keyboard if they recognized the word and the left arrow if they did not (i.e., if the word was not part of their vocabulary).

The mean word-recognition error rate for the controls was 2.75% and never exceeded 5%, and for the patients it was 13.3%. For 2 of the 6 patients, the rate was less than 5%, but the other 4 presented a mean of 19.3%. It was interesting to note that 78% of the errors committed involved non-words mistaken for real ones. Most of the non-words converted into words by the subjects with a history of hallucinations came from the NH list (83% v. 17% from the NA list). The results also showed that the subjects with a history of verbal auditory hallucinations were slower than controls in recognizing all words, regardless of the list

they belonged to. The median time required for patients to recognize a word was 1048.66 ms, and for controls, the time required was 679.91 ms ($p = 0.004$). Finally, the patients were significantly faster ($p \leq 0.001$) at recognizing the words from the H list than those from the A list (median time 823.25 ms for H list v. 943 ms for A list). Among controls, there was no significant difference between the amount of time required to recognize words from either list.

These results indicate that even during periods of full remission, patients are quicker to recognize words that are part of their hallucinations than those that are not. This corroborates the idea of a lexicon specific to hallucinated words that undergoes special cognitive processing by subjects during high-stress episodes.

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References

1. Sommer IEC, Aleman A, Kahn RS. Left with the voices of hearing right? Lateralization of auditory verbal hallucinations in schizophrenia [letter]. *J Psychiatry Neurosci* 2003;28(3):217-8.
2. Mendrek A, Laurens KR, Ngan E, Stip E, Kiehl KA, Liddle PF. New insights into prefrontal function in schizophrenia. *Schizophr Res* 2001;49 (Suppl 1-2):181.
3. Beaudot J. *Fréquence d'utilisation des mots en français écrit contemporain*. Montréal: Presse de l'Université de Montréal; 1992.